



Iovance Reports Updated IOV-LUN-202 Results and Adds Precision TIL Strategy for Second-Line Metastatic Non-Small-Cell Lung Cancer (mNSCLC)

October 29, 2026

24.6% Objective Response Rate (ORR) in 69 Patients with Non-Squamous mNSCLC, Consistent with Previously Reported Results

IOV-LUN-202 Cohorts 1 and 2 Are Completing Enrollment and Support a Planned Supplemental Biologics License Application (sBLA) for Lifileucel in Non-Squamous mNSCLC in 2027

KRAS Wild-Type Subgroup Achieved 43.3% ORR Versus 11.4% in KRAS-Mutant Disease and Novel Biomarker-Enriched Subgroup Achieved 59.1% ORR

POSITILITY, a First-In-Class Biomarker-Enriched Study with Registrational Intent, to Begin Enrollment in November 2026

PHILADELPHIA, Oct. 29, 2026 (GLOBE NEWSWIRE) -- Iovance Biotherapeutics, Inc. (NASDAQ: IOVA), a commercial biotechnology company developing and delivering tumor infiltrating lymphocyte (TIL) therapies for cancer, today announced updated results from Cohorts 1 and 2 of its Phase 2 IOV-LUN-202 trial and a first-in-class biomarker-enriched precision TIL strategy for lifileucel in previously treated non-squamous mNSCLC.

IOV-LUN-202 Cohorts 1 and 2 are completing enrollment and support the planned sBLA for lifileucel in non-squamous mNSCLC in 2027.

As of the October 14, 2026 data cutoff, 17 of 69 patients responded, representing an ORR of 24.6%, consistent with the 25.6% ORR previously reported in 39 patients.

A retrospective analysis identified a biomarker-enriched subgroup defined by Kirsten rat sarcoma viral oncogene homolog (*KRAS*) wild-type status, human epidermal growth factor receptor 2 (*HER2*) wild-type status, and current or former smoking. This subgroup represented less than one-third of the broader study population (22 of 69 patients) but accounted for more than three-quarters of the observed responses (13 of 17), with an ORR of 59.1% (13 of 22 patients).

The *KRAS* findings and further biomarker enrichment provide the clinical foundation for Iovance's precision TIL strategy. Iovance will prospectively evaluate this novel approach with POSITILITY, a first-in-class, prospective, biomarker-enriched cohort within the Phase 2 IOV-LUN-202 trial, designed with registrational intent.

Updated Results in the Broader Non-Squamous mNSCLC Population

Updated results from Cohorts 1 and 2 include 30 additional patients, bringing the total to 69 patients with non-squamous mNSCLC whose disease had progressed on or after platinum-based chemotherapy and immune checkpoint inhibitor therapy. Patients were enrolled without prospective selection using the novel biomarker-enrichment criteria.

The 17 reported responses included 15 confirmed responses and two unconfirmed partial responses (uPRs) awaiting confirmation. Radiologic assessments by an independent review committee are ongoing.

Response durability and the safety profile remained consistent with previous reports. The study incorporates an updated, reduced-dose lymphodepletion regimen that has improved the overall safety profile.

The broader IOV-LUN-202 Cohorts 1 and 2 are completing enrollment, with approximately 80 non-squamous NSCLC patients expected in the final dataset, and an sBLA for lifileucel in non-squamous mNSCLC is planned for 2027. Discussions with the U.S. Food and Drug Administration (FDA) are ongoing, and Iovance expects to provide further updates on the broader-population program in 2027.

KRAS Wild-Type Status Anchors the Precision TIL Strategy

To understand differences in response, Iovance evaluated clinical outcomes alongside tumor genomic and translational data. The analysis focused on tumor antigen presentation—the process by which tumor cells display targets for recognition by polyclonal TIL—and immune activity within the tumor microenvironment. Published preclinical studies in lung cancer models have linked oncogenic *KRAS* signaling to impaired antigen presentation and immune suppression, providing a biological rationale for investigating the association between *KRAS* status and response to lifileucel.¹

KRAS status emerged as the lead biomarker for Iovance's novel enrichment strategy. In the broader population of 69 patients with non-squamous mNSCLC, the ORR was 43.3% (13 of 30 patients) in the *KRAS* wild-type subgroup, compared with 11.4% (4 of 35 patients) in the *KRAS*-mutant subgroup. Both complete responses occurred in patients with *KRAS* wild-type tumors. These findings provided the rationale for further enrichment within the *KRAS* wild-type subgroup.

Building on this signal, Iovance incorporated *HER2* wild-type status and current or former smoking status into its enrichment strategy. These criteria draw on standard tumor genomic testing and routinely collected smoking history. Preclinical research suggests that aberrant *HER2* signaling can suppress antitumor immunity, while smoking-associated mutations generate additional tumor targets for recognition by polyclonal TIL.

All 13 responses in the *KRAS* wild-type subgroup occurred among the 22 patients meeting the combined enrichment criteria, yielding an ORR of 59.1%, including both complete responses. These patients represented 31.9% of the broader study population but accounted for 76.5% of the

observed responses. Together, the clinical findings and biological rationale support prospective evaluation of this combined enrichment strategy for lifileucel. The results for these populations are summarized in the following table.

Population	n	ORR*
Broader non-squamous NSCLC population	69	24.6% (17/69)
<i>KRAS</i> wild-type	30	43.3% (13/30)
<i>KRAS</i> -mutant	35	11.4% (4/35)
<i>KRAS</i> wild-type + <i>HER2</i> wild-type	25	52.0% (13/25)
<i>KRAS</i> wild-type + <i>HER2</i> wild-type + ever smoker	22	59.1% (13/22)

*ORRs include two uPRs, pending confirmation: one in the *KRAS* wild-type group and one in the *KRAS*-mutant group. Four *KRAS*-unassessed patients are excluded.

"These findings are reshaping how we develop TIL therapy for mNSCLC," said Frederick Vogt, Ph.D., J.D., Interim President and Chief Executive Officer of Iovance. "The expanded dataset reinforces the activity of lifileucel in previously treated disease, while the concentration of responses in *KRAS* wild-type tumors points to a more precision approach to patient selection. In the enriched subgroup, nearly six in ten patients responded, including two complete responses. We believe these insights could expand lifileucel's potential as a one-time treatment for mNSCLC, with a best-in-class profile compared to other therapies in development."

Iovance has launched POSITIVITY as a first-in-class, prospective, biomarker-enriched cohort within the ongoing IOV-LUN-202 program, with enrollment to begin in November 2026 at the first of over 70 existing IOV-LUN-202 sites. Iovance intends for the study to support a potential registrational pathway, subject to FDA feedback.

"Tumor-reactive T cells need recognizable targets and a tumor microenvironment that supports a sustained antitumor response," said Wayne Rothbaum, co-Chair of the Scientific Committee of Iovance's Board of Directors. "The response pattern in IOV-LUN-202 provided a clinical rationale for testing how tumor biology can guide TIL therapy. Starting with *KRAS* status, and refining selection through *HER2* status and smoking history, we identified a highly responsive mNSCLC subgroup where TIL biology converges with an immuno-reactive tumor microenvironment. We now aim to translate these novel findings into a precision development plan utilizing *KRAS*-based stratification, designed to identify patients most likely to benefit from lifileucel therapy."

Supporting Frontline Data and Development Plans

In a separate analysis of frontline Cohort 3A of IOV-COM-202, six of seven patients with non-squamous mNSCLC, *KRAS* wild-type tumors, and a current or former smoking history responded to lifileucel plus pembrolizumab (without chemotherapy), yielding an ORR of 85.7%. *HER2* status was not assessed in these patients. These findings provide additional rationale for prospective evaluation of lifileucel in the frontline setting.

Iovance plans to initiate OPTILISM, an innovative, frontline trial in biomarker-enriched non-squamous mNSCLC, in 2027. OPTILISM and the second-line POSITIVITY trial are intended to evaluate lifileucel across two treatment settings and assess the role of biomarker-guided patient selection within the mNSCLC development program.

Across the patient populations enrolling into OPTILISM and POSITIVITY, the prevalence of the biomarker-enriched population is estimated at approximately 45% of the cases of non-squamous mNSCLC diagnosed each year in the U.S., leading to more than 90,000 annual deaths and representing a significant market opportunity for lifileucel.

Additional details on the clinical results and development plans are available in a presentation posted to the Investor Relations section of www.iovance.com.

About IOV-LUN-202

IOV-LUN-202 is a Phase 2 study evaluating lifileucel in patients with previously treated mNSCLC. This update reports results from the 69 patients in Cohorts 1 and 2 with non-squamous histology who received a total viable cell count of at least 10 billion. Lifileucel remains investigational for the treatment of mNSCLC.

About Iovance Biotherapeutics

Iovance Biotherapeutics, Inc. is the global leader in innovating, developing, and delivering tumor infiltrating lymphocyte (TIL) cell therapies for patients with solid tumors. Amtagvi® (lifileucel) is the first FDA-approved, one-time treatment for previously treated advanced melanoma, now approved in three global markets and available at nearly 100 authorized treatment centers (ATCs). The Iovance TIL platform spans registrational trials and next-generation programs in additional solid tumors, including gene-edited and IL-12 tethered TIL therapies, next-generation IL-2, and precision immuno-oncology approaches. As the first and only company to take TIL therapy from concept to a broadly accessible commercial treatment, Iovance operates as an end-to-end cell therapy company, anchored by fully owned, centralized U.S.-based manufacturing that is scaled to serve thousands of cancer patients worldwide each year. Headquartered in Pennsylvania with offices and laboratories in California and Florida, Iovance serves patients at ATCs and clinical sites across almost the entire U.S. and in many countries around the world. For more information, please visit www.iovance.com.

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Iovance owns patent rights and other intellectual property rights related to the biomarker-directed strategy described in this press release. Information on Iovance's broad, industry-leading patent portfolio is available on the Intellectual Property page on www.iovance.com.

References

1. Mugarza E, et al. Therapeutic KRASG12C inhibition drives effective interferon-mediated antitumor immunity in immunogenic lung cancers. Science Advances. 2022;8:eabm8780. <https://doi.org/10.1126/sciadv.abm8780>

Forward-Looking Statements

Certain matters discussed in this press release are “forward-looking statements” of Iovance Biotherapeutics, Inc. (hereinafter referred to as the “Company,” “we,” “us,” or “our”) within the meaning of the Private Securities Litigation Reform Act of 1995 (the “PSLRA”). Without limiting the foregoing, we may, in some cases, use terms such as “predicts,” “believes,” “potential,” “continue,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “forecast,” “guidance,” “outlook,” “may,” “can,” “could,” “might,” “will,” “should,” or other words that convey uncertainty of future events or outcomes and are intended to identify forward-looking statements. Forward-looking statements are based on assumptions and assessments made in light of management’s experience and perception of historical trends, current conditions, expected future developments, and other factors believed to be appropriate. Forward-looking statements in this press release are made as of the date of this press release, and we undertake no duty to update or revise any such statements, whether as a result of new information, future events, or otherwise. Forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties, and other factors, many of which are outside of our control, that may cause actual results, levels of activity, performance, achievements, and developments to be materially different from those expressed in or implied by these forward-looking statements.

Important factors that could cause actual results, developments, and business decisions to differ materially from forward-looking statements are described in the sections titled “Risk Factors” in our filings with the U.S. Securities and Exchange Commission, including our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, and include, but are not limited to, the following substantial known and unknown risks and uncertainties inherent in our business: the risks related to our ability to successfully commercialize our products; the size of the addressable patient populations for, and the acceptance by the market of, our products and product candidates, if approved, and their potential pricing and/or reimbursement by payors, and whether such acceptance is sufficient to support continued commercialization or development of our products or product candidates; the risk regarding our ability to manufacture our therapies at our iCTC facility, including the risk that our ability to increase manufacturing capacity at our facility may adversely affect our commercial supply or clinical supply; the risks related to our ability to obtain, maintain and enforce patent and other intellectual property protection for our products and product candidates, including our biomarker-directed strategy; the risk that the successful development or commercialization of our products may not generate sufficient revenue from product sales, and we may not become profitable in the near term, or at all; the risks related to the timing of and our ability to successfully develop, submit, obtain, or maintain regulatory authority approval of our product candidates and any required companion diagnostics; whether clinical trial results from our clinical studies and cohorts, and meetings with regulatory authorities, may support registrational studies, including biomarker-selected studies such as POSITIVITY, and subsequent approvals by regulatory authorities, and the risk that our clinical trials, including registrational trials, may experience delays in site activation, enrollment, or data readouts, may not meet their primary endpoints, or may not support approval; clinical results, whether preliminary, interim, or final, which may include efficacy and safety results, from clinical trials or cohorts, including retrospective subgroup analyses, may not be confirmed or reflected in independent review assessments or the final analyses of our ongoing clinical trials or subgroups within these trials or in other prior or future trials or cohorts; the risk that we may be required to conduct additional clinical trials or modify ongoing or future clinical trials based on feedback from regulatory authorities; the risk that our interpretation of the results of our clinical trials, including comparisons to other therapies, or communications with regulatory authorities may differ from the interpretation of such results or communications by such regulatory authorities or others; the risk that clinical data from ongoing clinical trials of Amtagvi will not continue or be repeated in ongoing or planned clinical trials or may not support regulatory approval or renewal of authorization; the risk that unanticipated expenses may decrease our estimated cash balances and forecasts and increase our estimated capital requirements; the risk that we may not be able to recognize revenue for our products; the risk that Proleukin revenues, and other factors such as the number of ATCs, may not serve as a leading indicator for Amtagvi revenues; the risks regarding our anticipated operating and financial performance, including our financial guidance and projections; the effects of global and domestic geopolitical factors or public health events; and other factors, including general economic conditions and regulatory developments, not within our control.

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